

AMENDMENTS TO THE CLAIMS

1-6. (canceled)

7. (currently amended) A method to obtain a database of signal transduction protein localization profiles in response to toxic compounds, which method comprises

recording the intracellular localization pattern of at least one signal transduction protein in a cell type,

providing a set of toxic compounds,

contacting each compound of said set ~~a multiplicity of toxic compounds with at least one~~ said cell type,

~~observing and recording any translocation~~ the intracellular localization pattern of at least one of said signal transduction proteins in said cell type in the presence of each compound in said set of toxic compounds, optionally as a function of time,

wherein each intracellular localization pattern is constructed by concurrently determining the presence, absence or amount of said signal transduction protein in at least three cellular locations selected from the group consisting of nuclear, perinuclear, diffuse cytoplasmic, cytoplasmic fibril-associated, and membrane-associated locations;

~~wherein at least 2 cell types are employed and/or~~

~~the translocation of at least 2 signal transduction proteins is observed and/or~~

~~wherein the translocation is observed as a function of time; and~~

~~recording the observations of translocation~~

wherein each intracellular localization pattern is recorded in computer-readable and retrievable form.

8. (currently amended) The method of claim 7 wherein at least one of said signal transduction ~~protein~~ proteins is a protein kinase C (PKC) isoenzyme.

9. (currently amended) The method of claim 7 wherein the intracellular localization patterns of at least two signal transduction proteins [[is]] are determined.

10. (currently amended) The method of claim 9 wherein the intracellular localization patterns ~~localizations~~ of a multiplicity of signal transduction proteins ~~[[is]]~~ are determined.

11. (currently amended) The method of claim 7 wherein each of said ~~translocation~~ intracellular localization patterns is observed using a wide-field microscope.

12. (currently amended) The method of claim 7 wherein ~~the translocation is measured~~ each of said intracellular localization patterns is observed by labeling the proteins with specific antibodies.

13. (original) A computer-readable database prepared by the method of claim 7.

14-19. (canceled)

20. (currently amended) A method to identify a set of signal transduction proteins whose intracellular localization ~~is useful to determine perturbations from normal cellular status~~ pattern changes significantly in response to toxic compounds, which method comprises

- arbitrarily identifying an additional a first set of signal transduction proteins;
- providing a set of toxic compounds;
- contacting each member of said first set of signal transduction proteins with each one of the toxic compounds;
- determining the changes in intracellular localization pattern of each of the signal transduction proteins of said first set in response to an initial a set of arbitrarily chosen each of the toxic compounds which modify the status of the intracellular environment with respect to said initial set of signal transduction proteins;
- comparing the changes in intracellular localization obtained among members of the initial set of signal transduction proteins and compounds;
- discarding compounds and/or those signal transduction proteins from said first set which result in redundant intracellular translocation information whose changes in intracellular localization pattern are redundant;

~~substituting additional provisional~~ adding new signal transduction proteins and compounds for the proteins and compounds discarded to obtain a second set of proteins and a second set of compounds to provide a second set of signal transduction proteins;

contacting each member of said second set of signal transduction proteins with each of the toxic compounds;

~~obtaining intracellular localization information for the second set of compounds with respect to the second set of proteins;~~

determining the changes in the intracellular localization pattern of each of the signal transduction proteins of said second set in response to each of the toxic compounds;

discarding those signal transduction proteins from said second set whose changes in intracellular localization patterns are redundant; and

~~again comparing the intracellular localization information obtained among members of the initial set of signal transduction proteins and compounds, and~~

~~discarding compounds and proteins that result in redundant profiles; and~~

repeating the foregoing steps for which the second set of signal transduction proteins was used until a final set of proteins is obtained which provides at least five principal components with respect to the range of compounds marketed as small organic molecules.

21. (new) The method of claim 7, which further includes the step of recording the intracellular localization pattern of said signal transduction protein in said cell type in the presence of each compound of said set of toxic compounds as a function of time.

22. (new) The method of claim 7, which further includes the step of recording the intracellular localization pattern of said signal transduction protein in said cell type, then contacting each compound of said set of toxic compounds with a second cell type, and recording the intracellular localization pattern of said first signal transduction protein in said second cell type in the presence of each compound of said set of toxic compounds.